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Pharmaceuticals in our drinking water

### 66 Water, taken in moderation, cannot hurt anybody.??

-Mark Twain

### By Jackie Campbell, B.Sc. (Pharm.), LLB

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The above quote may no longer be true. Two recent Canadian publications highlight concerns about pharmaceuticals and personal care products (PCPs) such as shampoos, toothpaste, insect repellents, deodorants and perfumes in our water supply and their impact on drinking water safety and the aquatic environment.<sup>1,2</sup> Drugs are used to treat illnesses in humans and animals; they are also used in agriculture (e.g., as growth promoters in livestock) and aquaculture.<sup>1-3</sup> More than 23,000 drugs (consisting of at least 3,300 different ingredients) are registered in Canada.<sup>2</sup> Consumers are using more drugs than ever before: total sales in Canada of all drugs increased from \$6.6 billion to nearly \$13.8 billion between 1996 and 2004.<sup>4</sup> This article discusses the impact of human pharmaceutical contamination of our water supply, and focuses on the role that pharmacists can play in minimizing the environmental impact.

### How do drugs get into our water?

Drugs consumed by humans are eliminated (either unchanged or as metabolites) via flushing into the sewer or septic system (Figure 1). Consumers and healthcare professionals also discard outdated and unused drugs (including physician samples) down sinks and toilets into the sewer system or into landfill (regular garbage).<sup>2,5</sup> Most sewage is processed at sewage treatment plants (STPs) where it is separated into wastewater and solid (called biosolids, sludge) phases.<sup>2,6,7</sup> In some cases, raw sewage is piped directly into surface waters.<sup>5</sup>

Drugs can be broken down, remain as biosolids or dissolve in the liquid phase.<sup>2</sup> They may be degraded to some extent in STPs; however, many are detected in STP effluent that reaches ground and surface waters, suggesting that current technologies do not completely break down all drugs.<sup>2.6</sup> Wastewater from STPs is discharged into waterways, where it may be diluted (e.g., by a fast-flowing body of water) or remain concentrated (e.g., in a protected bay).<sup>7</sup> Biosolids and animal waste (e.g., manure from livestock) may be applied to fields as fertilizer; drugs in the excreta may leach into surface water via runoff or into ground water through infiltration.<sup>8</sup> Drugs used in aquaculture (e.g., fish farms) are released directly to surface water.<sup>9</sup>

## Which drugs get into the water?

Antibiotics, anti-inflammatories, antiepileptics, beta-blockers, lipid regulators, vasodilators and sympathomimetics have been detected in drinking water, groundwater, wastewater, sewage and STP influent/effluent.<sup>6,10</sup> This is not surprising, as cardiovascular drugs, psychotherapeutics, hormones, anti-infectives, cholesterol agents and analgesics were

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among the top 10 drugs classes in terms of total sales in Canada in 2005.<sup>11</sup>

Only a fraction of the drugs in use have been detected in surface waters. This is due, in part, to the low environmental concentrations of drugs (typical range is from parts per trillion [ng/L] to parts per billion [ug/L]) and analytical limitations in detecting them.<sup>2</sup>

#### What is the impact?

Even though most drugs break down over time through biological and photochemical processes, they are considered *persistent* due to the fact that they are continually discharged from sources such as STPs.<sup>2</sup> The impact of chronic exposure to low concentrations of drugs in the water on humans and nontarget plant and animal species is not known.

Drugs are designed to be both biologically active and rapidly eliminated in humans and animals. However, in species that are unable to metabolize and eliminate certain drugs, these agents may bioaccumulate (concentrate).<sup>12</sup> As well, some species may be sensitive to the effects of even very low concentrations of drugs. This is less likely in humans, who metabolize most drugs to more polar compounds that are less toxic and less active

figure 1

than the parent compounds.<sup>13</sup>

A recent study by Environment Canada found that municipal effluent from a primary STP entering the St. Lawrence River was cytotoxic to rainbow trout hepatocytes, the major drugmetabolizing cells in fish.<sup>12</sup> While the study did not find a direct relationship between the presence of pharmaceuticals in the water and toxicity, several drugs were detected in the effluent.

Fish may preferentially feed in nutrient-rich areas near STP outflows, where higher concentrations of pharmaceuticals are present.<sup>2</sup> Evidence suggests that subtle effects in fish, such as neurobehavioural changes, physical malformations and impaired development of the reproductive system may be related to trace pharmaceuticals.<sup>2</sup>

## Which drugs are of most concern?

While many drugs have been detected at low levels in water, their impact has not been adequately investigated, and establishing a causal relationship between drugs and specific toxicities is difficult.<sup>2</sup> However, there is evidence that estrogenic compounds may cause adverse effects, even at low levels of exposure.<sup>1,2</sup>



Adapted from: European Medicines Agency. Guideline on the environmental risk assessment of medicinal products for human use. June, 2006. www.emea.eu.int/pdfs/hman/swr/ 444700en.pdf (accessed October 23, 2006). In a federal government study in the Experimental Lakes Area in northwestern Ontario, ethinyl estradiol (EE) was added to a lake to achieve a concentration of 5–6 ng/L; this impaired male and female reproductive capacities in two minnow species, resulting in reproductive failure (a lethal effect). <sup>2,14,15</sup> Even low levels (0.1 ng/L) of EE have been shown to affect reproduction and gender ratios in fish near STPs.<sup>15</sup>

Continuous exposure to low concentrations of *antibiotics* in the environment, due to misuse or overuse by humans and use in animals, may promote the development of new strains of antibiotic-resistant bacteria.<sup>1,2</sup> Antibiotics may also affect the beneficial microbes necessary to break down organic matter in STPs.<sup>2</sup> Sensitization or development of an allergic response to antibiotics in the water supply may be an additional concern.<sup>16</sup>

## What is being done to minimize the impact?

**Environmental assessment:** Environment Canada and Health Canada are responsible for evaluating threats to human and environmental health posed by chemicals and other substances, and for taking measures to reduce risk.<sup>17,18</sup> In 2001, Health Canada began to develop environmental assessment regulations that will apply in the premarketing assessment of pharmaceuticals and PCPs.<sup>2,18</sup>

Model standards for permissible concentrations of pharmaceuticals in water supplies are already in place in Europe and the U.S., which Canada could choose to adopt. The European Medicines Agency (EMEA) recommends that an environmental risk assessment (requiring additional toxicological and environmental data) be undertaken for a drug whose predicted environmental concentration (PEC) in surface water is  $\geq 10$  ng/L.<sup>19</sup> This trigger concentration is a hundred times higher in the U.S. (i.e., less stringent), at 1 µg/L.<sup>20</sup> The validity of using standard trigger concentrations is questionable, mainly because there are so little data relating to toxic effects of drug residues on nontarget species. In

### Medicines should not be disposed of via wastewater or household waste.

addition, there are many unaccounted sources of drugs (e.g., illicit drugs, Internet sales, physician samples), and risk assessments typically do not account for drug metabolites or interactions among chemicals present in the "drug soup" in our water supply.<sup>8,20</sup> As well, lower trigger concentrations may be appropriate for some drugs, such as highly lipophilic agents or endocrine disruptors.<sup>19</sup>

**Research:** Environment Canada is spearheading ongoing studies to determine the types and amounts of drugs in STP effluent, sewage sludge and drinking water.<sup>2</sup>

*Municipal bylaws:* Municipalities have the authority to protect residents from material threats to their health and welfare.<sup>21</sup> For example, they can make bylaws prohibiting noncosmetic use of pesticides, as long as these bylaws do not breach federal or provincial laws.<sup>22</sup> Therefore, municipalities could adopt stricter sewer or garbage bylaws to regulate substances that may be disposed of via toilet, drain or landfill. Municipalities routinely ask citizens to bring hazardous wastes to depots rather than disposing in regular garbage; this could be expanded to include pharmaceuticals.

#### The pharmacist's role

Pharmacists can take steps to reduce environmental contamination by pharmaceuticals (Table 1).

Implement takeback/stewardship programs: National Association of Pharmacy Regulatory Authorities' (NAPRA) Model Standards of Practice for Canadian Pharmacists recommend that pharmacists accept the return of unused drugs for safe, appropriate disposal or redistribution.<sup>23</sup> Most provincial pharmacy licensing bodies across Canada encourage (but do not mandate) cradle-tograve care of pharmaceuticals by having the pharmacist accept the return of unused drugs for safe disposal.24 Detailed information on pharmacist standards of practice and takeback programs in Canada was published recently in Pharmacy Practice.<sup>25</sup> The Post Consumer Pharmaceutical Stewardship Association (PCPSA) also provides details on

available programs.<sup>26</sup> Funding mechanisms for such programs should be developed, including financial support from pharmaceutical manufacturers.

Advocate for standards: Pharmacists must demand that drinking water be as pristine and free from micropolludrugs are getting into our drinking water and providing a way for patients to dispose of unused drugs appropriately, pharmacists are communicating their concern for the environment. Ideally, pharmacies would provide a medication returns program that is simple for the

### table 1

# Pharmacist's role in ensuring appropriate drug disposal

- · Start or strengthen medication takeback programs
- Dispose of unused/outdated medications appropriately (e.g., via a waste management company)<sup>25</sup>
- Encourage wise medication use (e.g., discourage overprescribing and unnecessary OTC use)
- Educate consumers-provide handouts on proper drug disposal
- Include information on proper drug disposal in the pharmacy's own patient information leaflets
- Advocate for risk assessments and standards for drugs in the water supply

tants as possible. They could insist that the government require risk assessments regarding potential health and environmental impacts of new and existing substances. At a minimum, pharmacists should advocate that information about responsible disposal of drugs be mandated for inclusion in manufacturers' product monographs, on labels and in patient handouts. For example, the EMEA guidelines suggest that the following statement be included in patient information handouts: Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.<sup>19</sup>

**Educate patients:** Patients may not be aware that a pharmacy will take back unused medications. Pharmacy staff should inform the patients about what may be returned to the store.

### Conclusion

Pharmacists can take a role in minimizing drug contamination of our water supply. By informing patients of the fact that patient to understand, and accept all unused medications (including herbal and alternative medications), regardless of whether they were sold by that store.

To reinforce the message, pharmacists can provide patients with a handout about how to properly dispose of unused medications. Alternatively, a statement to this effect could be added to product information leaflets the pharmacy already provides to patients. Sample information sheets for use by patients and pharmacists regarding disposal of antibiotics and hormones are being drafted and will soon be posted on the Canadian Institute for Environmental Law and Policy website (www.cielap.org).<sup>27</sup>

We know very little about how drugs in our water supply affect humans, animals and plants. Even if cause and effect relationships are not fully established, precautionary measures are warranted when any activity raises threats of harm to human health or the environment.<sup>28</sup>

**References** available online at www.pharmacy gateway.ca (Go to Publication Archives, *Pharmacy Practice*, January 2007, Drugs on tap.)

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#### References

1. Holtz S. There is no "away." Pharmaceuticals. personal care products, and endocrine-disrupting substances: emerging contaminants detected in water. Canadian Institute for Environmental Law and Policy (CIELAP). January 2006:1-94. http://cielap.org/pdf/NoAway.pdf (accessed September 17, 2006). 2. Miller G. Environmental Commissioner of Ontario annual report 2004/05. October 2005:1-228. www.eco.on.ca/english/ publicat/ar2004.pdf (accessed September 17, 2006). 3. Health Canada. Veterinary drugs. Antimicrobial resistance 2003-01-06, www.hc-sc.gc. ca/dhp-mps/vet/faq/faq\_amr-ram\_e.html (accessed September 18, 2006). 4. NDMAC. A profile of the Canadian self-care health products market, July 2004. www.ndmac.ca/index.cfm? fuseaction=main.dspFile&FileID=120 (accessed October 22, 2006). 5. Daughton CG. Cradleto-cradle stewardship of drugs for minimizing their environmental disposition while promoting human health. II. Drug disposal, waste reduction, and future directions. Environ Health Perspect 2003;111:775-85. 6. Jjemba PK. Excretion and ecotoxicity of pharmaceutical and personal care products in the environment. Ecotoxicol Environ Safety 2006;63:113-30. 7. Miller G. Environmental Commissioner of Ontario annual report 2002/03. November, 2003:1-220. www. eco.on.ca/english/publicat/ar2002.pdf (accessed September 17, 2006), 8. Brecher R. Phillipps K. Pharmaceuticals in the environment, HazMat Management 2006 June/July;18(3):8-10. 9. Carlsson C, Johansson AK, Alvan G, et al. Are pharmaceuticals potent environmental pollutants? Part I: environmental risk assessments of selected active pharmaceutical ingredients. Sci Total Environ 2006;364:67-87. 10. Metcalfe CD, Koenig BG, Bennie DT, et al. Occurrence of neutral and acidic drugs in the effluents of Canadian sewage treatment plants. Environ Toxicol Chem 2003;22:2872-80. 11. IMS Health. Canada Rx Report 2005. www.imshealthcanada.com/ pharmafocus/pdf/FINAL\_Canada\_Rx\_Report\_ english.pdf (accessed September 18, 2006). 12. Gagné F, Blaise C, Andre C. Occurrence of pharmaceutical products in a municipal eff luent and toxicity to rainbow trout (Oncorhynchus mykiss) hepatocytes. Ecotoxicol Environ Safety 2006;64:329-36. 13. Food and Drug Administration. United States Department of Health and Human Services, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Guidance for Industry, Environmental Assessment of Human Drug and Biologics Applications. 1998 July:1-41. www.fda.gov/Cber/gdlns/environ.pdf (accessed September 18, 2006). 14. Lazorchak J, Flick R, Kidd K, et al. Fathead minnow and pearl dace pilot at Canadian Experimental Lakes Area. U.S. Environmental Protection Agency. EPA Science Forum 2005. www.epa.gov/nerl/news/forum 2005/lazorchak1.pdf#search=%22experimental %20lakes%20area%20estrogen%22 (accessed September 17, 2006). 15. European Medicines Agency (EMEA). Scientific discussion for the

approval of Evra. (undated):1-25. www.emea. eu.int/humandocs/PDFs/EPAR/evra/274802en6. pdf#search=%22This%20module%20reflects %20the%20initial%20scientific%20discussion %20for%20the%20approval%20of%20Evra. %20This%20scientific%22 (accessed September 18, 2006). 16. Jones OA, Lester JN, Voulvoulis N. Pharmaceuticals: a threat to drinking water? Trends in Biotechnology 2005;23:163-7. 17. Health Canada. Human health and the Canadian Environmental Protection Act (CEPA): an overview. Updated August 9, 2005. www. hc-sc.gc.ca/iyh-vsv/environ/cepalcpe\_e.html (accessed September 17, 2006). 18. Health Canada. Environmental impact initiative (September 26, 2006) www.hc-sc.gc.ca/ewhsemt/contaminants/person/impact/index\_e.html (accessed October 24, 2006). 19. European Medicines Agency (EMEA). Pre-authorisation evaluation of medicines for human use-guideline on the environmental risk assessment of medicinal products for human use, 2006 June; 1-12. www.emea.eu.int/pdfs/human/ swp/ 444700en.pdf (accessed October 23, 2006) 20. Daughton CG. Cradle-to-cradle stewardship of drugs for minimizing their environmental disposition while promoting human health. I. Rationale for and avenues toward a green pharmacy. Environ Health Perspect 2003;111:757-74. 21. See the "general welfare" provisions in municipal enabling statutes in various provinces, e.g. Quebec's Cities and Towns Act (R.S.Q., c. C-19, s. 410(1)) and Ontario's Municipal Act, 2001, (S.O. 2001, c. 24, s. 130). 22. See Spraytech v. Hudson [2001] 2 S.C.R. 241 (S.C.C.), where the Supreme Court of Canada upheld the town of Hudson's bylaw prohibiting cosmetic use of pesticides. A similar case in Ontario, Croplife Canada v. Toronto (City) (2005), 75 O.R. (3d) 357; (2005), 254 D.L.R. (4th) 40 (Ont. C.A.), extended this decision to the common law provinces. 23. National Association of Pharmacy Regulatory Authorities (NAPRA). Model standards of practice for Canadian pharmacists. (see, in particular, Operational component 5.5). www.napra. ca/practice/standards/standard5.html# 5-2-2 (accessed September 15, 2006). 24. National Association of Pharmacy Regulatory Authorities (NAPRA). Provincial and territorial regulatory authorities (various). www.napra.ca/ default.asp (click on each province) (accessed October 24, 2006). 25. Halasi S. Waste not, want not. A guide to appropriate disposal of used, expired or unwanted drugs. Pharm Pract 2005; 21(10):34-41. 26. Post Consumer Pharmaceutical Stewardship Association. Medications return program (provides information about provincial programs). www.medicationsreturn.ca/ and update bulletins www.medicationsreturn.ca/ bulletins/ (both accessed October 24, 2006). 27. Canadian Institute for Environmental Law and Policy (CIELAP). www.cielap.org/ (antibiotic/hormone disposal: sample information sheets to be posted in early 2007). 28. Kriebel D, Tickner J, Epstein P, et al. The precautionary principle in environmental science. Environ Health Perspect 2001;109:871-6.